

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently Amended) A nucleic acid construct for expression of a glucagon-like peptide-1 (GLP-1) or a variant ~~an analog~~ thereof, comprising:

a nucleic acid sequence encoding a signal peptide from the pre-region of somatostatin;

a nucleic acid sequence encoding the pro-region of a somatostatin, or a functional fragment of the pro-region of a somatostatin ~~sufficient to promote secretion from a cell~~, or a variant of the pro-region of a somatostatin wherein the functional fragment or variant differs from the wild-type amino acid sequence by at least 1 but not more than 5 ~~[[15]]~~ amino acid residues and is sufficient to promote secretion from a non-endocrine cell; and

a nucleic acid sequence encoding a GLP-1 or a variant ~~an analog~~ thereof.

2. (Currently Amended) The construct of claim 1, wherein the nucleic acid sequence encoding the signal peptide comprises ~~is from a nucleic acid sequence encoding~~ the pre-region of a somatostatin.

3.-5. (Canceled)

6. (Currently Amended) The construct of claim 1, wherein the construct further comprises a nucleotide sequence encoding a cleavage site between the sequence encoding the pro-region or functional fragment or variant thereof and the sequence encoding the GLP-1 or a variant ~~an analog~~ thereof.

7. (Canceled)
8. (Previously Presented) The construct of claim 6, wherein the cleavage site is a multibasic, dibasic or monobasic cleavage site.
9. (Previously Presented) The construct of claim 6, wherein the cleavage site is an endoprotease cleavage site.
10. (Previously Presented) The construct of claim 9, wherein the cleavage site is recognized by a pro-protein convertase.
11. (Original) The construct of claim 10, wherein the pro-protein convertase is furin, subtilisin-related pro-protein convertase, PC1, PC2, PC6 or PC7.
12. (Original) The construct of claim 1, further comprising at least one regulatory sequence.
13. (Canceled)
14. (Currently Amended) A non-endocrine cell comprising a nucleic acid sequence that encodes a fusion protein that comprises (a) a signal peptide from the pre-region of somatostatin, (b) a pro-region of a somatostatin or a functional fragment ~~of the pro-region of a somatostatin sufficient to promote secretion from a cell~~ or a variant of the pro-region of a somatostatin wherein the functional fragment or variant differs from the wild-type amino acid sequence by at least 1 but not more than 5 ~~[[15]]~~ amino acid residues and is sufficient to promote secretion from a non-endocrine cell, and (c) a glucagon-like peptide-1 (GLP-1) or a variant ~~an analog~~ thereof, the cell being capable of secreting the GLP-1 or variant ~~an analog~~ thereof.
- 15-16. (Canceled)

17. (Currently Amended) The cell of claim 14, wherein the encoded fusion protein further comprises a cleavage site between the pro-region or functional fragment or variant thereof and the GLP-1 or variant analog thereof.

18. (Canceled)

19. (Currently Amended) The cell of claim 14, wherein the cell is capable of expressing the GLP-1 or variant analog thereof in mature form without the signal peptide and pro-region of somatostatin or functional fragment or variant thereof.

20. (Canceled)

21. (Original) The cell of claim 14, wherein the cell is a primary cell.

22. (Original) The cell of claim 14, wherein the cell is a secondary cell.

23. (Original) The cell of claim 14, wherein the cell is a mammalian cell.

24. (Original) The cell of claim 23, wherein the cell is a human cell.

25. (Original) The cell of claim 23, wherein the cell is a fibroblast or a myoblast.

26. (Previously Presented) The cell of claim 14, wherein the cell is one in which somatostatin is not normally expressed.

27. (Previously presented) The cell of claim 14, wherein the nucleic acid sequence that encodes the fusion protein is operably linked to at least one regulatory sequence sufficient for expression of the fusion protein in the cell.

28.-31. (Canceled)

32. (Previously presented) The cell of claim 17, wherein the cleavage site is a multibasic, dibasic or monobasic cleavage site.

33. (Currently Amended) The cell of claim 17 ~~[[32]]~~, wherein the cleavage site is an endoprotease cleavage site.

34. (Previously Presented) The cell of claim 33, wherein the cleavage site is recognized by a pro-protein convertase.

35. (Original) The cell of claim 34, wherein the pro-protein convertase is furin, PACE4, subtilisin-related pro-protein convertase, PC1, PC2, PC6 or PC7.

36. (Previously presented) The cell of claim 17, wherein the cleavage site is a blood coagulation factor cleavage site.

37. (Canceled)

38. (Currently Amended) A method of making a GLP-1 or a variant ~~an analog~~ thereof comprising culturing the cell of claim 14 to thereby obtain GLP-1 or a variant ~~an analog~~ thereof.

39. (Currently Amended) The method of claim 38, wherein the GLP-1 or variant ~~analog~~ thereof is obtained in mature form without the signal peptide and pro-region of somatostatin or functional fragment or variant thereof.

40. (Currently Amended) The method of claim 38, wherein the GLP-1 or variant analog thereof is obtained as part of a fusion peptide which further comprises the pro-region of somatostatin or the ~~[[a]]~~ functional fragment or variant thereof.

41. (Currently Amended) A method of making a cell capable of secreting a GLP-1 or a variant ~~an analog~~ thereof, comprising:
providing a non-endocrine cell; and
introducing into the cell a nucleic acid construct of claim 1 or 6 to thereby obtain a cell capable of expressing the GLP-1 or variant ~~analog~~ thereof.

42. (Original) The method of claim 41, wherein the cell is a primary cell.

43. (Original) The method of claim 41, wherein the cell is a secondary cell.

44. (Original) The method of claim 41, wherein the cell is a mammalian cell.

45. (Currently Amended) The method of claim 41, wherein the sequence encoding the signal peptide comprises ~~is from the nucleic acid sequence encoding~~ the pre-region of a somatostatin.

46-82. (Canceled)

83. (Currently Amended) A nucleic acid construct for expression of GLP-1, comprising: a nucleic acid sequence encoding a fusion protein comprising a signal peptide from the pre-region of somatostatin; the pro-region of a somatostatin ~~or a functional fragment or variant thereof wherein the fragment or variant is sufficient to promote secretion from a cell and wherein the variant differs from the wild-type amino acid sequence by at least 1 but not more than 15 amino acid residues~~; and GLP-1.

84. (Currently Amended) A non-endocrine, mammalian cell comprising a nucleic acid sequence encoding a fusion protein comprising: a signal peptide from the pre-region of somatostatin, the pro-region of somatostatin, and a GLP-1, wherein the cell secretes the GLP-1.

85. (Canceled)

86. (Previously Presented) The cell of claim 84, wherein the cell is a human cell.

87. (Previously Presented) The cell of claim 84, wherein the cell is a fibroblast.

88. (Canceled)

89. (Previously Presented) A non-endocrine, human cell comprising a nucleic acid sequence encoding a fusion protein comprising: the prepro-region of somatostatin and GLP-1, wherein the cell secretes GLP-1.

90.- 93. (Canceled)

94. (New) A fibroblast comprising a nucleic acid sequence encoding a fusion protein comprising: the prepro-region of somatostatin and GLP-1 or a variant thereof, wherein the variant is selected from the group consisting of: GLP-1 (7-34), GLP-1 (7-35), GLP-1 (7-36), GLP-1 (7-37), Gln⁹-GLP-1 (7-37), Thr¹⁶-Lys¹⁸-GLP-1 (7-37), Lys¹⁸-GLP-1 (7-37), Gly⁸-GLP-1, Met¹⁶-Met²⁰-GLP-1 (7-37), and the cell secretes the GLP-1 or variant thereof.

95. (New) A method of making GLP-1 or a variant thereof comprising culturing the fibroblast of claim 94 to thereby obtain the GLP-1 or variant thereof.

96. (New) The construct of claim 1, wherein the variant is selected from the group consisting of: GLP-1 (7-34), GLP-1 (7-35), GLP-1 (7-36), GLP-1 (7-37), Gln⁹-GLP-1 (7-37), Thr¹⁶-Lys¹⁸-GLP-1 (7-37), Lys¹⁸-GLP-1 (7-37), Gly⁸-GLP-1, Met¹⁶-Met²⁰-GLP-1 (7-37).

97. (New) The cell of claim 14, wherein the variant is selected from the group consisting of: GLP-1 (7-34), GLP-1 (7-35), GLP-1 (7-36), GLP-1 (7-37), Gln⁹-GLP-1 (7-37), Thr¹⁶-Lys¹⁸-GLP-1 (7-37), Lys¹⁸-GLP-1 (7-37), Gly⁸-GLP-1, Met¹⁶-Met²⁰-GLP-1 (7-37).

98. (New) A nucleic acid construct for expression of GLP-1 comprising: a nucleic acid sequence encoding a fusion protein comprising the prepro-region of somatostatin and GLP-1.